```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:34:48 ON 23 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 23 Aug 2002  VOL 137 ISS 8
FILE LAST UPDATED: 21 Aug 2002  (20020821/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d que l19
L1             2 SEA FILE=REGISTRY TAUROLIDINE/CN OR "TAUROLIDINE NITRATE"/CN
L2           119 SEA FILE=HCAPLUS L1
L3            95 SEA FILE=HCAPLUS TAUROLIDINE
L4            43 SEA FILE=HCAPLUS TAUROLIN?
L5          3054 SEA FILE=HCAPLUS ?THIADIAZINE?
L6         18528 SEA FILE=HCAPLUS ?METHYLENEBIS?
L7            12 SEA FILE=HCAPLUS L5(L)L6
L8           142 SEA FILE=HCAPLUS L2 OR L3 OR L4 OR L7
L12           10 SEA FILE=HCAPLUS L8 AND RESISTAN?
L13           14 SEA FILE=HCAPLUS L8 AND STAPH?
L14            5 SEA FILE=HCAPLUS L8 AND VANCOMYCIN
L15            9 SEA FILE=HCAPLUS L8 AND TRANSFER?
L16           29 SEA FILE=HCAPLUS (L12 OR L13 OR L14 OR L15)
L17           53 SEA FILE=HCAPLUS L8 AND BACTERI?
L18            4 SEA FILE=HCAPLUS L17 AND (ADHES? OR ADHER?)
L19           31 SEA FILE=HCAPLUS L16 OR L18


=> d ibib abs l19 1-31

L19  ANSWER 1 OF 31  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:414500  HCAPLUS
TITLE:                    Antimicrobial activity of a novel catheter lock
                          solution
AUTHOR(S):                Shah, Chirag B.; Mittelman, Marc W.; Costerton, J. W.;
                          Parenteau, Stephen; Pelak, Michael; Arsenault,
                          Richard; Mermel, Leonard A.
CORPORATE SOURCE:         Biolink Corporation, Norwell, MA, USA
SOURCE:                   Antimicrobial Agents and Chemotherapy (2002), 46(6),
                          1674-1679
```

Search completed by David Schreiber 308-4292

CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intravascular catheter-assocd. bloodstream infections significantly increase rates of morbidity and hospital costs. Microbial colonization and development of biofilms, which are known to be recalcitrant to antibiotic therapy, often lead to the loss of otherwise patent vascular access systems. We evaluated a new **taurolidine**- and citrate-based catheter lock soln. (Neutrolin; Biolink Corporation, Norwell, Mass.) for its activity against planktonic microbes, antimicrobial activity in a catheter model, and biofilm eradication activity. In studies of planktonic microbes, after 24 h of contact, 675 mg of **taurolidine**-citrate soln. per L caused >99% redns. in the initial counts of **Staphylococcus** aureus, **Staphylococcus** epidermidis, Pseudomonas aeruginosa, and Entercoccus faecalis. A soln. of 13,500 mg/L was cidal for Candida albicans. Ports and attached catheters inoculated with 50 to 600 CFU of these bloodstream isolates per mL were locked with heparin or the **taurolidine**-citrate soln. After 72 h, there was no growth in the **taurolidine**-citrate-treated devices but the heparin-treated devices exhibited growth in the range of 6 .times. 102 to 5 .times. 106 CFU/mL. Biofilms were developed on silicone disks in modified Robbins devices with broth contg. 6% serum (initial counts, 106 to 108 CFU/cm2). The axenic biofilms were treated for 24 h with **taurolidine**-citrate or heparin. **Taurolidine** -citrate exposure resulted in a median redn. of 4.8 logs, whereas heparin treatment resulted in a median redn. of 1.7 logs ($P < 0.01$). No significant differences in the effects of the two treatments against P. aeruginosa and C. albicans were obsd. These findings suggest that **taurolidine**-citrate is a promising combination agent for the prevention and treatment of intravascular catheter-related infections.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:406928 HCAPLUS
DOCUMENT NUMBER: 136:363829
TITLE: Combination of fluorouracil and a methylol **transfer** agent for the treatment of tumor metastases and cancer
INVENTOR(S): Redmond, Paul H.; Pfirrmann, Rolf W.
PATENT ASSIGNEE(S): Ed Geistlich Soehne Ag Fuer Chemische Industrie, Switz.
SOURCE: Eur. Pat. Appl., 4 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1208840	A2	20020529	EP 2001-309983	20011128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002111328	A1	20020815	US 2001-993896	20011127

PRIORITY APPLN. INFO.: US 2000-253138P P 20001128

AB Tumor growth and metastases in cancer patients are inhibited by administration of a combination therapy including effective amts. of 5-FU

and a methylol **transfer** agent such as **taurolidine**, taurultam or mixts. thereof.

L19 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:392134 HCAPLUS
DOCUMENT NUMBER: 136:391028
TITLE: Aerosolized anti-infectives, anti-inflammatories, and decongestants for the treatment of sinusitis
INVENTOR(S): Osbakken, Robert S.; Hale, Mary Anne; Leivo, Frederick T.; Munk, James D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 577,623.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061281	A1	20020523	US 2001-942959	20010831
WO 2001002024	A1	20010111	WO 2000-US18410	20000705

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-142618P	P	19990706
US 1999-142620P	P	19990706
US 1999-142621P	P	19990706
US 1999-142622P	P	19990706
US 1999-142624P	P	19990706
US 1999-142741P	P	19990706
US 1999-142881P	P	19990706
US 2000-193507P	P	20000403
US 2000-193508P	P	20000403
US 2000-193509P	P	20000403
US 2000-193510P	P	20000403
US 2000-194078P	P	20000403
US 2000-577623	A2	20000525
WO 2000-US18410	A2	20000705

AB Pharmaceutical compns. are described that comprise one or more active ingredients selected from the group consisting of an anti-infective agent, anti-inflammatory agent, anti-mucolytic agent, antihistamine, an antiseptic, and antibiotic combinations or combinations of others of these classes of ingredients, and particularly to compns. formulated as a soln. or suspension in a unit dose for aerosol administration to treat chronic sinusitis. An aerosol is effective to kill at least about 90% of pathogens causing sinusitis in a patient within about 21 days when administrate every 8, 12, or 24 h. For example, a female patient with sinusitis triggered by allergies is usually treated with antihistamines and decongestants when allergies triggered headaches and/or a clear nasal discharge. Historically, she would have one or more sinus infections a year requiring twenty or more days of oral antibiotics. She was treated

with cefuroxime 285 mg in 2.5 mL of sterile water for injection three times daily using a nebulizer cup with adult mask attached and a turbo compressor. The patient experienced a dumping of green, purulent nasal discharge after eight treatments. The therapy was continued for a total of seven days. No other antibiotics were given. This patient remained free from sinus infections for six mo.

L19 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:351199 HCAPLUS
DOCUMENT NUMBER: 136:395392
TITLE: A randomized double-blinded placebo-controlled crossover trial of nebulized **taurolidine** in adult cystic fibrosis patients infected with Burkholderia cepacia
AUTHOR(S): Ledson, Martin J.; Gallagher, Malcolm J.; Robinson, Maxine; Cowperthwaite, Carolyn; Williets, Trevor; Hart, Charles A.; Walshaw, Martin J.
CORPORATE SOURCE: The Regional Adult Cystic Fibrosis Unit, Liverpool University, Liverpool, UK
SOURCE: Journal of Aerosol Medicine (2002), 15(1), 51-57
CODEN: JAEMEP; ISSN: 0894-2684
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Burkholderia cepacia is an aggressive pathogen that colonizes cystic fibrosis (CF) patients, causing greatly increased morbidity and mortality. It is **resistant** to most antibiotics, but sensitive in vitro to a novel agent, **taurolidine**. This has not previously been used against B. cepacia, nor given in nebulized form. We assessed the effect of nebulized **taurolidine** on United Kingdom epidemic (ET12) B. cepacia infection in 20 adult CF patients attending our regional adult cystic fibrosis outpatient clinic using a prospective, randomized, double-blinded placebo-controlled crossover trial. Nebulized **taurolidine** (4 mL 2% soln.) or saline (4 mL 0.9% soln.) was given twice daily. Each arm lasted 4 wk, with a 2-wk intervening washout period. Sputum B. cepacia colony counts (primary outcome measure), spirometry, and symptoms (secondary outcome measures) were assessed. Eighteen patients completed the study. There was no change in B. cepacia colony counts or spirometry, nor symptom scores. We conclude that, although **taurolidine** is well tolerated in nebulized form, in this study it had no in vivo anti-B. cepacia activity.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:330202 HCAPLUS
DOCUMENT NUMBER: 136:335222
TITLE: Treatment of tumor metastases and cancer with interleukin 2 and methylol **transfer** agent
INVENTOR(S): Redmond, H. Paul; Pfirrmann, Rolf W.
PATENT ASSIGNEE(S): Ed Geistlich Soehne A.-G. fuer Chemische Industrie, Switz.
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1201247	A2	20020502	EP 2001-309157	20011029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002098164	A1	20020725	US 2001-983279	20011023

PRIORITY APPLN. INFO.: US 2000-243409P P 20001027

AB Tumor metastases in cancer patients are inhibited by administration of a combination therapy including effective amts. of Interleukin-2 and a methylol **transfer** agent such as **taurolidine**, taurultam or mixts. thereof.

L19 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:151537 HCAPLUS
DOCUMENT NUMBER: 136:178023
TITLE: Compositions and methods for treating infections of the ear
INVENTOR(S): Costin, James C.
PATENT ASSIGNEE(S): Carter-Wallace, Inc., USA
SOURCE: U.S., 5 pp., Cont.-in-part of U.S. Ser. No. 151,885. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6350742	B1	20020226	US 1999-266056	19990310

PRIORITY APPLN. INFO.: US 1998-151885 A2 19980911

AB This invention provides methods and compns. for the treatment of bacterial infection referred to as otitis media or otitis externa presenting as inflammation of the mucosal lining of the external and/or middle ear usually with exudation which compns. in addn. to killing and eradicating pathogens also reduce or eliminate the ability of pathogens to acquire **resistance** to antibiotic drug treatment. Specifically, the present invention relates to the use of **taurolidine** [4,4-**methylenebis**(tetrahydro-1,2,4-**thiadiazine**-1,2-dioxide)] in treating infections of the ear.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:712133 HCAPLUS
DOCUMENT NUMBER: 136:48131
TITLE: **Taurolidine**: cytotoxic and mechanistic evaluation of a novel antineoplastic agent
AUTHOR(S): Calabresi, Paul; Goulette, Frederick A.; Darnowski, James W.
CORPORATE SOURCE: Department of Medicine, Division of Clinical Pharmacology, Brown University and Rhode Island Hospital, Providence, RI, 02903, USA
SOURCE: Cancer Research (2001), 61(18), 6816-6821 CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bis-(1,1-dioxoperhydro-1,2,4-thiadiazinyl-4)methane (**taurolidine**) is a synthetic broad-spectrum antibiotic that reacts with

bacterial cell membrane components to prevent **adhesion** to epithelial cell surfaces. Reflecting the key role of **adhesion** in the growth and development of human solid tumors, studies were initiated to assess the antiproliferative activity of this agent in selected human and murine tumor cell lines. A 3-day exposure to **Taurolidine** inhibited the growth of all of the cell lines evaluated with IC50s ranging from 9.6-34.2 .mu.M. Studies to identify the mechanism responsible for this effect were conducted in NIH-3T3 murine fibroblasts and the PA-1 and SKOV-3 human ovarian tumor cell lines. These studies revealed that a 48-h exposure to **taurolidine** had little effect on cell cycle distribution in PA-1 and SKOV-3 cells but significantly increased the appearance of DNA debris in the sub-G0/G1 region, an effect consistent with an induction of apoptosis. In contrast, in NIH-3T3 cells, **taurolidine** exposure did not increase DNA debris in the sub-G0/G1 region. Addnl. studies assessed phosphatidylserine externalization after a 24-h exposure to **taurolidine** using annexin-V binding as a cell surface marker. These studies revealed that **taurolidine** increased the percentage of annexin-V-pos. cells by 4-fold and 3-fold in PA-1 and SKOV-3 cells, resp. In NIH-3T3 cells, **taurolidine** exposure slightly increased (.apprx.5%) annexin-V binding. Parallel studies revealed that exposure to **taurolidine** also resulted in poly(ADP-ribose) polymerase cleavage in both ovarian tumor cell lines but not in NIH-3T3 cells. Finally, murine-based studies were conducted to assess the antineoplastic activity of three consecutive daily i.p. bolus injections of **taurolidine** at doses ranging from 5-mg injection/mouse to 30-mg injection/mouse. The 20-mg injection dose produced .apprx.10% mortality and was identified as the maximally tolerated dose in this model. Administration of this regimen to nude mice bearing i.p. human ovarian tumor xenografts significantly inhibited both tumor formation and growth. These findings are discussed in light of their clin. implications.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:524655 HCAPLUS
DOCUMENT NUMBER: 135:87183
TITLE: Methylol **transfer** agent for the treatment of inflammatory bowel disease
INVENTOR(S): Redmond, H. Paul; Pfirrmann, Rolf W.
PATENT ASSIGNEE(S): Ed. Geistlich Sohne A.-G. Fur Chemische Industrie, Switz.
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1116488	A2	20010718	EP 2001-300093	20010105
EP 1116488	A3	20020515		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002004502	A1	20020110	US 2001-753679	20010104
JP 2001226291	A2	20010821	JP 2001-739	20010105

PRIORITY APPLN. INFO.: US 2000-174608P P 20000105
AB Patients suffering from inflammatory bowel disease, e.g. Crohn's disease

or ulcerative colitis, are treated either orally or i.v. with methylol **transfer** agents, such as **taurolidine** and/or taurultam. These agents can be used in combination with other drugs, thereby allowing the use of smaller amts. of other drugs and limiting unwanted side effects.

L19 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:524654 HCAPLUS
DOCUMENT NUMBER: 135:87181
TITLE: Methylol **transfer** agent for reduction of postoperative complications of cardiopulmonary bypass surgery
INVENTOR(S): Redmond, H. Paul; Pfirrmann, Rolf W.
PATENT ASSIGNEE(S): Ed. Geistlich Sohne A.-G. Fur Chemische Industrie, Switz.
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1116487	A2	20010718	EP 2001-300092	20010105
EP 1116487	A3	20020417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002035996	A1	20020328	US 2001-753719	20010104
JP 2001247480	A2	20010911	JP 2001-740	20010105

PRIORITY APPLN. INFO.: US 2000-174606P P 20000105
US 2000-245235P P 20001103

AB The invention provides a method of reducing postoperative complications of cardiopulmonary bypass (CPB) surgery in which an effective amt. of a methylol **transfer** agent, e.g. **taurolidine**, is administered to a patient in conjunction with CPB surgery. Patients undergoing crystalloid cardioplegia who were treated with **taurolidine** showed reduced levels of IL-6 and increased levels of IL-10 when compared to crystalloid patients administered a placebo. Soln. formulations are included.

L19 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:416759 HCAPLUS
DOCUMENT NUMBER: 135:14312
TITLE: Use of methylol-containing compounds to treat tumors by inducing apoptosis
INVENTOR(S): Calabresi, Paul; Darnowski, James; Costin, James
PATENT ASSIGNEE(S): Rhode Island Hospital, A Lifespan Partner, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001039763	A2	20010607	WO 2000-US33104	20001206
WO 2001039763	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002049200	A1	20020425	US 2000-731214	20001206
US 2002052366	A1	20020502	US 2000-730666	20001206
US 6429224	B1	20020806	US 2000-730923	20001206
US 2002111345	A1	20020815		

PRIORITY APPLN. INFO.: US 1999-169122P A1 19991206
US 1999-169127P A1 19991206
US 1999-169128P A1 19991206

OTHER SOURCE(S): MARPAT 135:14312

AB The invention provides a method of inhibiting tumor growth in a mammal, by administering to the mammal a compn. contg. a methylol-contg. compd., e.g. **taurolidine**, taurultam, or a biol. active deriv. thereof. The compn. is administered to directly contact a tumor cell at a dose sufficient to induce cell death by apoptosis. **Taurolidine** selectively inhibited tumor cell growth and specifically induced apoptosis in tumor cells in mice. The cytotoxic IC50 of **taurolidine** was in the 10-50 .mu.M range, approx. 100-fold lower than that required for its antibiotic effects.

L19 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:28569 HCAPLUS
DOCUMENT NUMBER: 134:105843
TITLE: Methylol **transfer** agents **taurolidine** and taurultam for treating primary and secondary tumors of the central nervous system (CNS)
INVENTOR(S): Stendel, Rudiger; Pfirrmann, Rolf Wilhelm
PATENT ASSIGNEE(S): Ed. Geistlich Sohne A.-G. fuer Chemische Industrie, Switz.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1066830	A2	20010110	EP 2000-304737	20000605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2310534	AA	20001204	CA 2000-2310534	20000602
JP 2001010976	A2	20010116	JP 2000-168053	20000605

PRIORITY APPLN. INFO.: US 1999-137421P P 19990604
US 1999-151050P P 19990827
US 1999-167681P P 19991129
US 2000-174607P P 20000105
US 2000-182200P P 20000214

AB Methods and compns. for the treatment, prophylaxis, and/or suppression of primary and/or secondary tumors of the CNS (brain and spinal cord, eyes) in mammalian subjects using a methylol agent are described. An ED of a methylol **transfer** agent, such as **taurolidine** and/or

taurultam and/or a bioequivalent, is administered to a mammalian subject suffering from, or at risk of growth of, tumors of the central nervous system. Furthermore, methods for local application of **taurolidine** and/or taurultam and/or a bioequivalent in soln. are disclosed using microdialysis methods, irrigation methods, implantation methods and angiog. methods. The soln. for delivery to a patient should contain an effective dosage of **taurolidine** and/or taurultam and/or taurultam-glucose, e.g., in the tissue-culture of glioblastoma multiform-tumor cells, as little as 0.1-4 mg/mL **taurolidine** inhibits or kills tumor cells. Taurultam so far has been shown to be almost twice as effective as **taurolidine**, the explanation of which may be found in the equil. of **taurolidine** in aq. soln. between methylol-taurultam and taurultam. Taurultam-glucose, on the other hand, has to be dosaged about twice as high as taurultam, as the mol. wt. from taurultam increases from 136 to 298. When administered to patients utilizing the irrigation/catheter method, a concn. of at least about 4 mg/mL **taurolidine**, taurultam or taurultam-glucose, resp., should be utilized.

L19 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:367626 HCAPLUS
DOCUMENT NUMBER: 133:117336
TITLE: Activities of **taurolidine** in vitro and in experimental enterococcal endocarditis
AUTHOR(S): Torres-Viera, C.; Thauvin-Eliopoulos, C.; Souli, M.; DeGirolami, P.; Farris, M. G.; Wennersten, C. B.; Sofia, R. D.; Eliopoulos, G. M.
CORPORATE SOURCE: Departments of Medicine and Pathology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(6), 1720-1724
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vitro, the antimicrobial agent **taurolidine** inhibited virtually all of the bacteria tested, including **vancomycin-resistant** enterococci, oxacillin-**resistant staphylococci**, and Stenotrophomonas maltophilia, at concns. between 250 and 2,000 .mu.g/mL. **Taurolidine** was not effective in exptl. endocarditis. While it appears unlikely that this antimicrobial would be useful for systemic therapy, its bactericidal activity and the **resistance** rates found (<10-9) are favorable indicators for its possible development for topical use.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:451194 HCAPLUS
DOCUMENT NUMBER: 131:68124
TITLE: Use of antimicrobial agent such as **taurolidine** or taurultam in the manufacture of a medicament to treat a nosocomial microbial infection
INVENTOR(S): Pfirrmann, Rolf
PATENT ASSIGNEE(S): Ed Geistlich Sohne A.-G. fur Chemische Industrie, Switz.; Pett, Christopher
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9934805	A1	19990715	WO 1999-GB28	19990106
W: AU, CA, CN, JP, KR, RU				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5972933	A	19991026	US 1998-4063	19980108
CA 2317748	AA	19990715	CA 1999-2317748	19990106
AU 9918844	A1	19990726	AU 1999-18844	19990106
EP 1044006	A1	20001018	EP 1999-900217	19990106
R: DE, ES, FR, GB, IT				
JP 2002500189	T2	20020108	JP 2000-527254	19990106

PRIORITY APPLN. INFO.: US 1998-4063 A 19980108
WO 1999-GB28 W 19990106

AB The invention provides a method and compn. for treatment of a nosocomial, microbial infection of a patient which comprises introduction into the gut of a patient an antimicrobial amt. of an antimicrobial medicament which is cell wall constituent-inactivating, endotoxin non-releasing, exotoxin-inactivating, or a combination thereof. In particular, the invention provides the use of **taurolidine** and/or taurultam in the treatment of multi-**resistant** infections, e.g. **vancomycin-resistant** Enterococcus faecalis and methicillin-**resistant Staphylococcus** aureus.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:419569 HCAPLUS
DOCUMENT NUMBER: 131:71129
TITLE: Inactivation of **staphylocoagulase** by **taurolin**
AUTHOR(S): Reinmuller, Johannes; Mutschler, W.; Meyer, H.
CORPORATE SOURCE: Klinik Sonnenberg, Wiesbaden, D-65191, Germany
SOURCE: Haemostaseologie (Stuttgart) (1999), 19(2), 94-97
CODEN: HAEMD2; ISSN: 0720-9355
PUBLISHER: F. K. Schattauer Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: German

AB **Taurolin**, a chemotherapeutic agent with bactericidal and antitoxic properties, is used successfully in surgery of bacterial infections, esp. the chronic state of osteitis. However, the antitoxic activity was predominantly reported of the endotoxins of gram-neg. bacteria. Now it was demonstrated that **taurolin** inhibits the **staphylocoagulase**-induced clotting of citrate blood plasma. **Staphylocoagulase** is a factor which is released by the gram-pos. bacterial species **Staphylococcus** aureus. The inactivation effect is dependent on the **taurolin** concn. and could be detected below the minimal inhibitory concn. for S. aureus. Addnl. inactivation could be attained by increasing the time the **staphylocoagulase** was exposed to the agent. These exptl. findings strongly support the view that **taurolin** acts by chem. modification of the bacterial protein via methylol **transfer**. As **staphylocoagulase** is the major characteristic of the pathogenic **Staphylococcus** species we it was assumed that its inactivation is an important feature of

the efficiency of **taurolin** in the treatment or **staphylococcal** infections.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:31552 HCAPLUS
DOCUMENT NUMBER: 130:204819
TITLE: Tumor necrosis factor-.alpha. production by human hepatoma cell lines is **resistant** to drugs that are inhibitory to macrophages
AUTHOR(S): Wordemann, Meike; Fandrey, Joachim; Jelkmann, Wolfgang
CORPORATE SOURCE: Inst. of Physiology, Medical Univ., Luebeck, Germany
SOURCE: Journal of Interferon and Cytokine Research (1998), 18(12), 1069-1075
CODEN: JICRFJ; ISSN: 1079-9907
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Little is known about the potential of immunomodulatory agents to lower tumor necrosis factor-.alpha. (TNF-.alpha.) synthesis in tissues of non-monocytic origin. The authors studied effects of diverse drugs on the formation of immunoreactive TNF-.alpha. in the human hepatoma cell lines HepG2 and Hep3B, in which TNF-.alpha. prodn. was induced by treatment (3 h incubation periods) with interleukin-1.beta. (IL-1.beta., 300 pg/mL) or phorbol myristate acetate (PMA, 100 nmol/L). TNF-.alpha. prodn. in IL-1.beta.-stimulated or PMA-stimulated hepatocyte cultures was not altered following the addn. of dihydrocortisone (.ltoreq.1 .mu.g/mL), dibutyryl-cAMP (db-cAMP, .ltoreq.100 .mu.mol/l), adenosine (.ltoreq.1 mmol/l), thalidomide (.ltoreq.25 .mu.g/mL), or cyclosporine (.ltoreq.300 ng/mL). TNF-.alpha. prodn. was inhibited by **taurolidine** (.gtoreq.300 .mu.g/mL), but this inhibition was assocd. with reduced cell viability. Pentoxifylline (1 mg/mL) did not influence PMA-induced TNF-.alpha. prodn., but it augmented IL-1.beta.-induced TNF-.alpha. prodn. Measurements of TNF-.alpha. mRNA by RT-PCR indicated that pentoxifylline exerted its effect posttranscriptionally. Addnl. studies with PMA-treated human whole blood cultures confirmed that pentoxifylline, db-cAMP, and adenosine reduced TNF-.alpha. prodn. by leukocytes. These results provide first evidence to assume cell type-specific effects of immunomodulatory drugs on TNF-.alpha. synthesis, which may be relevant with respect to their clin. application.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:549468 HCAPLUS
DOCUMENT NUMBER: 127:145180
TITLE: Agent for prevention of tumor cell **transfer** and growth of trocar metastases in open and laparoscopic surgery of malignant tumors
INVENTOR(S): Mueller, Joachim Michael; Jacobi, Christoph Andreas
PATENT ASSIGNEE(S): Mueller, Joachim Michael, Germany; Jacobi, Christoph Andreas
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19606897	A1	19970814	DE 1996-19606897	19960213

AB Development of trocar metastases is inhibited by administration of **taurolidine**, alone or combined with heparin or heparin derivs. Thus, growth and adherence of colon carcinoma cells in vitro was inhibited by **taurolidine** (300 .mu.L 2% soln./mL growth medium).

L19 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:183009 HCAPLUS
DOCUMENT NUMBER: 120:183009
TITLE: Treatment of dentoalveolar infections with **taurolidine** and/or taurultam
INVENTOR(S): Pfirrmann, Rolf Wilhelm; Geistlich, Peter
PATENT ASSIGNEE(S): Holmes, Michael John, UK; Ed Geistlich Soehne AG fuer Chemische Industrie
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403174	A1	19940217	WO 1993-GB1607	19930729
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 652753	A1	19950517	EP 1993-917947	19930729
R: AT, BE, DE, ES, FR, GB, IT, NL				
JP 07509483	T2	19951019	JP 1993-505094	19930729
PRIORITY APPLN. INFO.:			GB 1992-16155	19920730
			WO 1993-GB1607	19930729

AB The present invention provides a new means of combating severe dentoalveolar infections such as dental gangrene, parodontitis and abscesses which involves the administration of the methylol-**transfer** agents **taurolidine** and/or taurultam. In one embodiment the **taurolidine** and/or taurultam compns. may be administered prophylactically to combat post-operative infection. Certain novel compns. comprising **taurolidine** and or taurultam are also described. Patients with alveolitis sicca dolorose, gangrene, parodontitis marginalis, pericoronitis, abscess, and infection were treated with **taurolidine** in an irrigation fluid, in a liq. gel, and in a dental emulsion, all at 3%. **Taurolidine** was superior to the std. therapy for all 6 indications.

L19 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:535437 HCAPLUS
DOCUMENT NUMBER: 119:135437
TITLE: **Taurolidine**: in vitro activity against multiple-antibiotic-**resistant**, nosocomially significant clinical isolates of **Staphylococcus** aureus, Enterococcus faecium, and diverse Enterobacteriaceae
AUTHOR(S): Traub, Walter H.; Leonhard, Birgit; Bauer, Dierk
CORPORATE SOURCE: Inst. Med. Mikrobiol. Hyg., Univ. Saarlandes, Homburg/Saar, Germany
SOURCE: Chemotherapy (Basel) (1993), 39(5), 322-30

Search completed by David Schreiber 308-4292

CODEN: CHTHBK; ISSN: 0009-3157
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Taurolidine** at .ltoreq.1,250 .mu.g/mL killed all 37 isolates of multiple-antibiotic-**resistant Staphylococcus** aureus (n = 9), Enterococcus faecium (n = 17), and Enterobacteriaceae (n = 11). Time-kill expts. disclosed that bovine serum (65% vol./vol.) only marginally retarded the bactericidal activity of 2000 and 1000 .mu.g/mL of **taurolidine** against the various strains. **Taurolidine** at 2000 .mu.g/mL did not antagonize the bactericidal activity of 50% (vol./vol.) fresh human serum against promptly and delayed serum-sensitive test strains of Escherichia coli and Serratia marcescens. In the presence of 65% (vol./vol.) of fresh defibrinated human blood from two donors, however, the bactericidal activity of this antimicrobial compd. was delayed, i.e., manifested only following extended (overnight) incubation, against **staphylococcal** and enterococcal isolates, through less so in the case of Enterobacteriaceae. **Taurolidine** at 2000 .mu.g/mL killed ingested, i.e., intraphagocytic bacteria of human-serum-**resistant** S. marcescens strains CDC 06:H3 and P 016:H-.

L19 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:467886 HCAPLUS
DOCUMENT NUMBER: 119:67886
TITLE: Enterococcus faecium: in vitro activity of antimicrobial drugs, singly and combined, with and without defibrinated human blood, against multiple-antibiotic-**resistant** strains
AUTHOR(S): Traub, Walter H.; Leonhard, Birgit; Bauer, Dierk
CORPORATE SOURCE: Inst. Med. Mikrobiol. Hyg., Univ. Saarlandes, Homburg/Saar, Germany
SOURCE: Chemotherapy (Basel) (1993), 39(4), 254-64
CODEN: CHTHBK; ISSN: 0009-3157
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The minimal inhibitory (MICs) and bactericidal concns. of 14 antimicrobial drugs were detd. against 17 clin. isolates of Enterococcus faecium, including 4 glycopeptide-**resistant** strains. Both teicoplanin and **vancomycin** lacked bactericidal activity against all 13 susceptible isolates. Time-kill expts. served to test various antibiotic combinations chiefly against glycopeptide-**resistant** strains in Mueller-Hinton broth (MHB) and in MHB supplemented with 65% (vol./vol.) fresh defibrinated human blood. Cotrimoxazole, fusidic acid, and novobiocin yielded bacteriostatic effects. Rifampin was bactericidally active against rifampin-susceptible strains (MICs = 0.125 .mu.g/mL), but less so against low-level rifampin-**resistant** (MICs = 2-8 .mu.g/mL) strains in MHB. However, in the presence of human blood, rifampin (2 .mu.g/mL) combined with cotrimoxazole (0.25/4.75 .mu.g/mL) killed rifampin-susceptible and low-level-rifampin-**resistant**, but not moderate-level-rifampin-**resistant** (MICs = 16-32 .mu.g/mL) strains of E. faecium. Of two topical drugs examd., mupirocin merely inhibited strains of E. faecium; conversely, **taurolidine** at 2000 .mu.g/mL was efficacious against all strains examd., although the kinetics of bactericidal activity were retarded somewhat in the presence of 65 vol% human blood.

L19 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:104129 HCAPLUS
DOCUMENT NUMBER: 116:104129
TITLE: **Taurolidine**, an analog of the amino acid

taurine, suppresses interleukin 1 and tumor necrosis factor synthesis in human peripheral blood mononuclear cells
AUTHOR(S): Bedrosian, Isabelle; Sofia, R. Duane; Wolff, Sheldon M.; Dinarello, Charles A.
CORPORATE SOURCE: Dep. Med., New England Med. Cent., Boston, MA, 02111, USA
SOURCE: Cytokine (Philadelphia) (1991), 3(6), 568-75
CODEN: CYTIE9; ISSN: 1043-4666
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Taurolidine** (Geistlich Pharm, AG, Wolhusen, Switzerland), a deriv. of the amino acid taurine, is used as an adjunctive therapy for various infections. The ability of I to block lipopolysaccharide (LPS)-induced tumor necrosis factor (TNF) and interleukin 1 (IL-1) synthesis was examd. in human peripheral blood mononuclear cells (PBMC). There was a dose-dependent redn. in the synthesis of these 2 cytokines when I was preincubated with LPS before being added to PBMC. This redn. was independent of the molar ratio of I to LPS but was related to the concn. of I present in the PBMC cultures. There was a 80-90% redn. in total IL-1 and TNF synthesis induced by LPS at concns. of I of 4-100 .mu.g/mL; the vehicle was without effect. Following a 30-min preincubation with PBMC, I could be washed from the cells and still suppress cytokine synthesis induced by LPS. A dose of 100 .mu.g/mL of I was not toxic for PBMC. I also reduced IL-1 and TNF synthesis induced by the **Staphylococcus** species. Thus, I blocks the prodn. of IL-1 and TNF in human PBMC; furthermore, the protective effect of I may, in part, be due to its ability to reduce IL-1 and TNF synthesis during infection.

L19 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:651972 HCAPLUS
DOCUMENT NUMBER: 115:251972
TITLE: The effects of three non-antibiotic, antimicrobial agents on the surface hydrophobicity of certain microorganisms evaluated by different methods
AUTHOR(S): Jones, D. S.; Gorman, S. P.; McCafferty, D. F.; Woolfson, A. D.
CORPORATE SOURCE: Sch. Pharm., Queen's Univ. Belfast, Belfast, UK
SOURCE: J. Appl. Bacteriol. (1991), 71(3), 218-27
CODEN: JABAA4; ISSN: 0021-8847
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of 3 nonantibiotic, antimicrobial agents (**taurolidine**, chlorhexidine acetate and providone-iodine) on the surface hydrophobicity of the clin. strains Escherichia coli, **Staphylococcus** saprophyticus, **Staphylococcus** epidermidis, and Candida albicans were examd. Three recognized techniques for hydrophobicity measurements, **Bacterial Adherence** to Hydrocarbons (BATH), the Salt Aggregation Test (SAT) and Hydrophobic Interaction Chromatog. (HIC) were compared. At concns. reported to interfere with microbial-epithelial cell **adherence**, all 3 agents altered the cell surface hydrophobicity. However, these effects failed to exhibit a uniform relationship. Generally, **taurolidine** and povidone-iodine treatments decreased the hydrophobicity of the strains examd. whereas chlorhexidine acetate effects depended upon the microorganism treated. Subsequently, the exact contribution of altered cell surface hydrophobicity to the reported microbial anti-**adherence** effects is unclear. Comparison of the 3 techniques

revealed a better correlation between the results obtained with the BATH test and HIC than the results obtained with the BATH and SAT or SAT and HIC. However, these differences may be due to the inaccuracy assocd. with the visual assessment of results employed by the SAT.

L19 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:39096 HCAPLUS
DOCUMENT NUMBER: 114:39096
TITLE: In vitro antibacterial activity of noxythiolin and **taurolidine**
AUTHOR(S): Blenkharn, J. Ian
CORPORATE SOURCE: R. Postgrad. Med. Sch., Hammersmith Hosp., London, W12 0NN, UK
SOURCE: J. Pharm. Pharmacol. (1990), 42(8), 589-90
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The min. inhibitory concns. (MIC) of noxythiolin and **taurolidine** were detd. for strains of **Staphylococcus** aureus, Escherichia coli and Pseudomonas aeurginosa. Tests were performed in broth alone and in broth plus 25% serum or 25% urine. Inoculum d. was wither 103, 105 or 107 colony-forming units per mL-1. Slight inoculum-dependent variation in the activity of both agents was obsd. for some, but not all, strains of P. aeruginosa and S. aureus. A more pronounced medium-dependent increase in activity was obsd. with both drugs, with up to 8-fold redn. of values for MIC when tested in the presence of serum or urine. These observations may help to clarify the disparity between the obsd. clin. efficacy of these agents and relatively poor in vitro activity when tested using conventional methods in synthetic media.

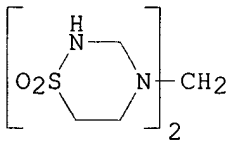
L19 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:205119 HCAPLUS
DOCUMENT NUMBER: 110:205119
TITLE: In vitro anti-leishmanial activity of compounds in current clinical use for unrelated diseases
AUTHOR(S): Neal, R. A.; Allen, S.
CORPORATE SOURCE: Dep. Med. Protozool., London Sch. Hyg. Trop. Med., St. Albans/Herts., UK
SOURCE: Drugs Exp. Clin. Res. (1988), 14(10), 621-8
CODEN: DECRDP; ISSN: 0378-6501
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Drugs in current clin. use were tested for anti-Leishmania activity using an in vitro infected macrophage assay. Out of almost 400 compds. tested, over 100 were active. The most active compds. showed ED50 values below 1 .mu.M. The active compds. should be tested in in vivo systems. They made lead to the development of new antileishmanials.

L19 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:101948 HCAPLUS
DOCUMENT NUMBER: 110:101948
TITLE: Polarographic analysis of **taurolidine**, a non-antibiotic antimicrobial agent
AUTHOR(S): Woolfson, A. D.; McCafferty, D. F.; Gorman, S. P.; Jones, D. S.
CORPORATE SOURCE: Dep. Pharm., Queen's Univ. Belfast, Belfast, UK
SOURCE: Int. J. Pharm. (1988), 48(1-3), 167-72
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal

Search completed by David Schreiber 308-4292

White 09/915,121

LANGUAGE: English
GI



I

AB The behavior in aq. soln. of the non-antibiotic antimicrobial agent, **taurolidine** (I), which has marked anti-adherence properties, was investigated by differential pulse polarog. (DPP). I gave well-defined differential pulse polarograms at pH 4.2 with a peak potential of -0.83 V vs. Ag/AgCl. This behavior was identical to that of aq. taurultam solns. A comparison of peak current ratios, cyclic voltammograms and peak potential/pH plots confirmed that the I signal was due to the redn. of taurultam and its hydroxymethyl deriv. A mechanism for the cathodic redn. of taurultam was proposed involving a 2-electron **transfer**. The signal at -0.83 V was of anal. utility, but was lost at alk. pH. A second peak appeared in the polarogram for **taurolidine** solns. at alk. pH and was identified as HCHO. This was quantified by a rapid DPP method. Only trace amts. of HCHO were found in com. I (**Taurolin**) solns. and these were of no clin. significance.

L19 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:4536 HCAPLUS
DOCUMENT NUMBER: 110:4536
TITLE: Inhibition by formaldehyde condensates of microbial adherence to human mucosal epithelial cells: clinical implications
AUTHOR(S): Gorman, S. P.; McCafferty, D. F.; Woolfson, A. D.; Anderson, L.; Jones, D. S.
CORPORATE SOURCE: Med. Biol. Cent., Queens Univ. Belfast, Belfast, BT9 7BL, UK
SOURCE: U. S. Environ. Prot. Agency, Res. Dev., [Rep.] EPA (1987), EPA/600/9-87/031, Proc.: Conf. Prog. Chem. Disinfect., 3rd, 1986, 372-85
CODEN: XPARD6; ISSN: 0092-8054
DOCUMENT TYPE: Report
LANGUAGE: English
AB The effects of the broad spectrum antimicrobial agents noxythiolin and **taurolidine** (urea-formaldehyde condensates) on mucosal adherence of Candida albicans, Escherichia coli, and **Staphylococcus** saprophyticus were studied in vitro on human epithelial cells collected from the mouth and voided urine. Both agents reduced the adherence in both exponential and stationary growth phases of the microorganisms. Formaldehyde in clin. relevant concns. and N-methylthiourea had no antiadherent effect.

L19 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:470269 HCAPLUS
DOCUMENT NUMBER: 109:70269
TITLE: Sustained anti-**adherence** activity of **taurolidine** (**Taurolin**) and noxythiolin (Noxyflex S) solutions
AUTHOR(S): Blenkharn, J. Ian

Search completed by David Schreiber 308-4292

CORPORATE SOURCE: R. Postgrad. Med. Sch., Hammersmith Hosp., London, W12 0HS, UK
SOURCE: J. Pharm. Pharmacol. (1988), 40(7), 509-11
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Taurolidine** (2% w/v) and noxythiolin (1% w/v and 2.5% w/v) solns. inhibit the **adherence** in vitro of Escherichia coli and **Staphylococcus** aureus to human epithelial and fibroblast cells. This effect, demonstrable after 30 min exposure of cells to test drugs, persists after removal of the active compd. Significantly reduced **adherence** of **bacteria** is apparent for 5 h after **taurolidine** treatment and for 6 h after treatment with 2.5% noxythiolin. The anti-**adherence** activity of **taurolidine** and noxythiolin may contribute to the obsd. clin. efficacy of these agents.

L19 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:87643 HCAPLUS
DOCUMENT NUMBER: 108:87643
TITLE: A comparative study of the microbial anti-**adherence** capacities of three antimicrobial agents
AUTHOR(S): Gorman, S. P.; McCafferty, D. F.; Woolfson, A. D.; Jones, D. S.
CORPORATE SOURCE: Med. Biol. Cent., Queen's Univ. Belfast, Belfast, BT9 7BL, UK
SOURCE: J. Clin. Pharm. Ther. (1987), 12(6), 393-9
CODEN: JCPTED; ISSN: 0269-4727
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antimicrobial agents, **taurolidine**, chlorhexidine, and providone-iodine were examd. for microbial anti-**adherence** activity in 2 **adherence** systems: an oral isolate of Candida albicans to human buccal epithelial cells and of a urine isolate of Escherichia coli to human uroepithelial cells. Each of the agents exhibited anti-**adherence** activity, which was concn. dependent. The activity was expressed at subminimum inhibitory concns. of the agents. Treatment of either the microbial or epithelial cells resulted in redns. in **adhering** microorganisms. The agents exhibited a broadly based antiadherence capacity. Anti-**adherence** agents may have a potential role in the prophylaxis of infection.

L19 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:451465 HCAPLUS
DOCUMENT NUMBER: 107:51465
TITLE: Reduced adherence of microorganisms to human mucosal epithelial cells following treatment with **Taurolin**, a novel antimicrobial agent
AUTHOR(S): Gorman, S. P.; McCafferty, D. F.; Woolfson, A. D.; Jones, D. S.
CORPORATE SOURCE: Med. Biol. Cent., Queen's Univ. Belfast, Belfast, BT9 7BL, UK
SOURCE: J. Appl. Bacteriol. (1987), 62(4), 315-20
CODEN: JABAA4; ISSN: 0021-8847
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Taurolin** (**taurolidine**) reduced the adherence of buccal and vaginal strains of Candida albicans blastospores and urine isolates of

Escherichia coli and **Staphylococcus** saprophyticus to uroepithelial or buccal epithelial cells. A max. redn. in adherence of .apprx.65% was obtained. The antiadherence capacity was time-dependent, requiring a contact time of 30 min to achieve max. effect. **Taurolin** at less than the min. inhibitory concns. (MIC) significantly reduced the adherence of Candida and E. coli. A concn. slightly higher than the MIC was required for S. saprophyticus. Treatment of either the epithelial cells or the microorganisms with **Taurolin** resulted in reduced adherence of the microorganisms.

L19 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:172802 HCAPLUS
DOCUMENT NUMBER: 106:172802
TITLE: The antimicrobial activity of **Taurolin** - a possible additive for parenteral nutrition solutions
AUTHOR(S): Blenkharn, J. I.
CORPORATE SOURCE: R. Postgraduate Med. Sch., Hammersmith Hosp., London, W12 OHS, UK
SOURCE: Clin. Nutr. (1987), 6(1), 35-8
CODEN: CLNUDP; ISSN: 0261-5614
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The anti-**staphylococcal** activity of **Taurolin**, a broad spectrum, non-toxic antimicrobial, was evaluated. There was no adverse interaction with commonly used parenteral nutrition fluids, including lipid emulsions. The apparent safety of **Taurolin** and lack of pharmaceutical interaction suggests that the incorporation of this compd. at a final concn. of 3 g/L may protect against the frequent septic complications assocd. with **staphylococcal** contamination of parenteral nutrition solns. during pharmaceutical prepn. and assembly of the fluid administration set.

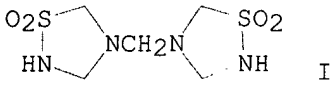
L19 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:610950 HCAPLUS
DOCUMENT NUMBER: 103:210950
TITLE: **Taurolin**-bacteriology in vitro
AUTHOR(S): Brodhage, H.; Pfirrmann, R. W.
CORPORATE SOURCE: Meggen, CH-6045, Switz.
SOURCE: Taurolin (1985), 38-47. Editor(s): Brueckner, Walter, L; Pfirrmann, Rolf W. Urban & Schwarzenberg: Munich, Fed. Rep. Ger.
CODEN: 54MRAY
DOCUMENT TYPE: Conference
LANGUAGE: German
AB The in vitro activity of **taurolin**, a synthetic antimicrobial, was detd. against various species of bacteria, mycobacteria, and fungi. The antibacterial effect of **taurolin** was greatest at low pH (5) and was unaffected by serum. No significant **resistance** to **taurolin** developed after 25-30 subcultures of **Staphylococcus** aureus or Escherichia coli.

L19 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:115123 HCAPLUS
DOCUMENT NUMBER: 86:115123
TITLE: **Taurolin**, a new chemotherapeutic agent
AUTHOR(S): Browne, M. K.; Leslie, G. B.; Pfirrmann, R. W.
CORPORATE SOURCE: Dep. Surg., Glasgow R. Infirm., Glasgow, Scot.
SOURCE: J. Appl. Bacteriol. (1976), 41(3), 363-8
CODEN: JABAA4

Search completed by David Schreiber 308-4292

White 09/915,121

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB **Taurolin** (bis-(1,1-dioxoperhydro-1,2,4-thiadiazinyl-4)-methan)(I) [**19388-87-5**] was effective in mice against a wide range of pathogenic organisms including Pseudomonas aeruginosa, Escherichia coli, Proteus vulgaris, and Salmonella typhimurium, and would be of particular use against antibiotic-**resistant** organisms. It is based on an endogenous substance, taurine, which acts as a nontoxic formaldehyde carrier donating methylol groups to bacterial protein and endotoxin, thus causing denaturation and polycondensation of the pathogens and their pyrogens. It is anticipated that Taurollin will be of value in the treatment of fecal peritonitis.

Search completed by David Schreiber 308-4292

```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:40:11 ON 23 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 23 Aug 2002  VOL 137 ISS 8
FILE LAST UPDATED: 21 Aug 2002  (20020821/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d que l22
L1             2 SEA FILE=REGISTRY TAUROLIDINE/CN OR "TAUROLIDINE NITRATE"/CN
L2           119 SEA FILE=HCAPLUS L1
L3            95 SEA FILE=HCAPLUS TAUROLIDINE
L4            43 SEA FILE=HCAPLUS TAUROLIN?
L5          3054 SEA FILE=HCAPLUS ?THIADIAZINE?
L6         18528 SEA FILE=HCAPLUS ?METHYLENEBIS?
L7            12 SEA FILE=HCAPLUS L5(L)L6
L8           142 SEA FILE=HCAPLUS L2 OR L3 OR L4 OR L7
L12           10 SEA FILE=HCAPLUS L8 AND RESISTAN?
L13           14 SEA FILE=HCAPLUS L8 AND STAPH?
L14            5 SEA FILE=HCAPLUS L8 AND VANCOMYCIN
L15            9 SEA FILE=HCAPLUS L8 AND TRANSFER?
L16           29 SEA FILE=HCAPLUS (L12 OR L13 OR L14 OR L15)
L17           53 SEA FILE=HCAPLUS L8 AND BACTERI?
L18            4 SEA FILE=HCAPLUS L17 AND (ADHES? OR ADHER?)
L19           31 SEA FILE=HCAPLUS L16 OR L18
L20           18 SEA FILE=HCAPLUS COSTIN J?/AU
L21            4 SEA FILE=HCAPLUS L20 AND L8
L22            2 SEA FILE=HCAPLUS L21 NOT L19


=> d ibib abs l22 1-2

L22  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:575759  HCAPLUS
TITLE:                    Taurolidine compositions and methods for
                          treating superficial fungal infections
INVENTOR(S):              Costin, James C.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 6 pp., Division of U.S. Ser.
```

No. 568,635, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103187	A1	20020801	US 2001-945638	20010904
US 6436926	B1	20020820		

PRIORITY APPLN. INFO.: US 1999-133283P P 19990510
US 2000-568635 B3 20000510

AB Compns. comprising 4,4'-**methylenebis**(tetrahydro-1,2,4-**thiadiazine**) 1,1,1',1',-tetraoxide and their use in treating dermatol. disorders are disclosed.

L22 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:468209 HCAPLUS
DOCUMENT NUMBER: 135:56076
TITLE: Compositions and methods for the management of Crohn's disease using **taurolidine** formulations
INVENTOR(S): **Costin, James C.**
PATENT ASSIGNEE(S): Carter-Wallace, Inc., USA
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6251896	B1	20010626	US 2000-535477	20000324

PRIORITY APPLN. INFO.: US 1999-125880P P 19990324

AB The present invention relates to a method of treating a human infected with Crohn's disease comprising enterally administering to the individual in need of such treatment an effective amt. of a compn. comprising 4,4'-**methylenebis**(tetrahydro-1,2,4-**thiadiazine**)-1,1,1',1'-tetraoxide, commonly known as.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search completed by David Schreiber 308-4292